Nos. 24-2274, 24-2277, 24-2278

United States Court of Appeals for the Federal Circuit

JAZZ PHARMACEUTICALS, INC.,
Plaintiff-Appellee,

v.

AVADEL CNS PHARMACEUTICALS, LLC,
Defendant-Appellant.

JAZZ PHARMACEUTICALS, INC.,
JAZZ PHARMACEUTICALS IRELAND LIMITED,
Plaintiffs-Appellees,

v.

AVADEL CNS PHARMACEUTICALS, LLC,
Defendant-Appellant.

JAZZ PHARMACEUTICALS, INC.,
JAZZ PHARMACEUTICALS IRELAND LIMITED,
Plaintiffs-Appellees,

v.

AVADEL CNS PHARMACEUTICALS, LLC,
Defendant-Appellant.

Appeals from the U.S. District Court for the District of Delaware,
Nos. 21-0691, 21-1138, 21-1594, Hon. Gregory B. Williams

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CERTIFICATE OF INTEREST

Case Numbers: 24-2274, 24-2277, 24-2278

Short Case Caption: *Jazz Pharmaceuticals, Inc. v. Avadel CNS Pharmaceuticals, LLC*

Filing Party/Entity: Avadel CNS Pharmaceuticals, LLC, Defendant-Appellant

I certify the following information and any attached sheets are accurate and complete to the best of my knowledge.

Date: November 18, 2024 Signature: */s/ Gabriel K. Bell*
Name: Gabriel K. Bell

1. Represented Entities. Provide the full names of all entities represented by undersigned counsel in this case. Fed. Cir. R. 47.4(a)(1).

Avadel CNS Pharmaceuticals, LLC

2. Real Party in Interest. Provide the full names of all real parties in interest for the entities. Do not list the real parties if they are the same as the entities. Fed. Cir. R. 47.4(a)(2).

None.

3. Parent Corporations and Stockholders. Provide the full names of all parent corporations for the entities and all publicly held companies that own 10% or more stock in the entities. Fed. Cir. R. 47.4(a)(3).

Avadel CNS Pharmaceuticals, LLC is wholly owned subsidiary of Avadel US Holdings, Inc., which is a wholly owned subsidiary of Avadel Pharmaceuticals plc. Avadel Pharmaceuticals plc is a publicly traded company with no parent corporation. Janus Henderson Group plc, a publicly traded company, owns more than 10% of Avadel Pharmaceuticals plc's stock.

4. Legal Representatives. List all law firms, partners, and associates that (a) appeared for the entities in the originating court or agency or (b) are expected to appear in this court for the entities. Do not include those who have already entered an appearance in this court. Fed. Cir. R. 47.4(a)(4).

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5. Related Cases. Other than the originating case(s) for this case, are there related or prior cases that meet the criteria under Fed. Cir. R. 47.5(a)?

Yes.

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None/Not Applicable.

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INTRODUCTION

Jazz mounts no serious defense on the merits of the district court's sweeping injunction, which forbids Avadel from exercising its lawful rights to seek FDA approval and conduct clinical trials for such approval—as secured by the Patent Act's safe harbor. Instead, Jazz characterizes Avadel's merits argument regarding the scope of the injunction as an "affirmative defense" and asserts that Avadel somehow waived that defense or failed to adduce factual support for it. Jazz is wrong on both counts. Avadel's merits argument is not an affirmative defense in this case, but rather a pure legal argument about the limits on the district court's injunction authority in the face of the safe harbor. Avadel presented its argument in the district court, and Jazz affirmatively disclaimed any intention of seeking an injunction that would violate the safe harbor. Indeed, Jazz represented that it "*never disputed* that Avadel could conduct … studies" for "idiopathic hypersomnia ('IH')." Appx7367 n.1 (emphasis added). Jazz cannot about-face to evade review now. The question whether the injunction violates the safe harbor is properly before this Court.

And on the merits, there is no real question that the injunction violates the safe harbor. So Jazz now stretches even further, insisting that the district court was free to enjoin conduct *even if* it falls within the safe harbor. But Congress anticipated that attempted end-run: "*no injunctive or other relief* may be granted which would prohibit" safe harbor conduct. 35 U.S.C. § 271(e)(3) (emphasis added). This is just

Jazz's latest attempt to twist the statutory scheme and frustrate FDA's consideration of new, competing treatments that can benefit patients and the public. This Court rejected such an attempt last time, *Jazz Pharms., Inc. v. Avadel CNS Pharms., LLC*, 60 F.4th 1373, 1380-81 (Fed. Cir. 2023), and should do so again. The injunction unambiguously reaches heartland safe harbor conduct. That alone warrants reversal.

Jazz's defense of the district court's *eBay* factor analysis fares no better. Like the district court, Jazz identifies no irreparable harm. There is no risk from Avadel seeking FDA approval for an IH indication and conducting clinical trials, and any commercial sales by Avadel are years away. Also, there is simply no way to meaningfully evaluate the public interest when the injunction *prevents* FDA from making findings that would undoubtedly impact that analysis. Indeed, FDA's findings were the cornerstone of the district court's (correct) determination that enjoining Avadel's FDA-approved narcolepsy treatment *would* injure the public. That dissonance highlights the danger—and legal error—in granting an injunction based on hypothetical events that are years away.

The district court's injunction should be reversed.

ARGUMENT

I. THE INJUNCTION IMPROPERLY PROHIBITS SAFE HARBOR ACTIVITY THAT CANNOT BE ENJOINED AS A MATTER OF LAW

The injunction exceeds the scope of the district court's authority because it sweeps in activities that the Patent Act expressly deems non-infringing by prohibiting Avadel from seeking FDA approval and conducting clinical trials for an IH indication. *See* Avadel Br. 21-26, 29-32; 35 U.S.C. § 271(e)(1).

As Avadel explained, the safe harbor in Section 271(e)(1) "provides a wide berth" that "extends to *all* uses of patented inventions that are reasonably related to the development and submission of *any* information under the FDCA [Food, Drug, and Cosmetic Act]." *Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193, 202 (2005) (first emphasis added); *see* Avadel Br. 3-7. This Court routinely holds "as a matter of law" that the safe harbor protects "acts or uses that bear a reasonable relation to the development and submission of information to the FDA"—i.e., "'[a]s long as [the] activity is reasonably related to obtaining FDA approval.'" *Edwards Lifesciences Corp. v. Meril Life Scis. Pvt. Ltd.*, 96 F.4th 1347, 1352-53 (Fed. Cir. 2024) (emphasis and citation omitted); *see also Classen Immunotherapies, Inc. v. Elan Pharms., Inc.*, 786 F.3d 892, 894, 897 (Fed. Cir. 2015).

The safe harbor applies here. Seeking FDA approval for an IH indication is not just "reasonably related" to the "submission of information" to FDA; it *is* the submission of information to FDA. *See* 35 U.S.C. § 271(e)(1). And both the

ongoing REVITALYZ trial (including its open-label extension period) and any future clinical trials that Avadel might conduct to support its request for FDA approval for an IH indication are, by definition, the "development … of information" for FDA, *id.*—"activity squarely within the safe harbor," *Edwards*, 96 F.4th at 1352. That is enough to decide this case. Because the safe harbor applies, the district court lacks authority to enjoin these non-infringing activities. Avadel Br. 21; *see also Int'l Rectifier Corp. v. IXYS Corp*., 383 F.3d 1312, 1316 (Fed. Cir. 2004) ("[T]he only acts the injunction may prohibit are infringement of the patent ...."); 35 U.S.C. § 271(e)(3) ("no injunctive or other relief may be granted" prohibiting safe harbor activities). Tellingly, the district court's order never—not once—tried to reconcile the scope of its injunction with the statutory safe harbor.

A. Jazz's Merits Arguments Fail On Their Face

Jazz's attempts to defend the merits of the district court's restrictions on safe harbor activities are foreclosed by the plain statutory text and binding law.

1. Jazz first argues that the safe-harbor inquiry in this case is factual rather than legal. Jazz Br. 42-43. Not so. This case presents a straightforward legal question: Whether seeking FDA approval and conducting clinical trials for FDA approval qualify as "uses reasonably related to the development and submission of information" to FDA. 35 U.S.C. § 271(e)(1). Merely asking that question answers

it: Yes, as a matter of law. Because the injunction prohibits those activities, the district court exceeded its authority by entering the injunction. Avadel Br. 21-26.

Jazz is wrong that the application of the safe harbor is in this case (and always) a "'factual issue' requiring the presentation of evidence." Jazz Br. 42. The Supreme Court and this Court routinely interpret the safe harbor's text and determine whether activity is protected as a matter of law. *See, e.g.*, *Merck*, 545 U.S. at 208 ("adopt[ing]" a "construction of § 271(e)(1)"); *Edwards*, 96 F.4th at 1353 (resolving safe-harbor protection "as a matter of law"). So while the "contours of [the safe-harbor] provision are not exact *in every respect*, the statutory text makes clear that it provides a wide berth for the use of patented drugs in activities related to the federal regulatory process." *Merck*, 545 U.S. at 202 (emphasis added). And in *this* case, and in *these respects*, the statute is crystal clear: Seeking FDA approval and conducting clinical trials for that FDA submission are "reasonably related" to developing and submitting information to FDA. Not just that—they *are* the development and submission of information to FDA.

The Supreme Court's jurisprudence confirms that the issue presented can be resolved as a matter of law in these circumstances. In *Merck*, the Court "construed" the safe harbor and held that it was not "limit[ed] … to the development of information for inclusion in a submission to the FDA," 545 U.S. at 206-07—such that even "preclinical research" where the "results … are not ultimately included in

a submission to [FDA]" could not be categorically excluded from the safe harbor, *id.* at 195. Likewise, in *Eli Lilly & Co. v. Medtronic, Inc.*, the Court considered the "proper interpretation" of the safe harbor and concluded that, as a matter of law, the phrase "'patented invention'" includes "all inventions, not drug-related inventions alone." 496 U.S. 661, 665 (1990). It thus categorically determined that certain inventions come within the safe harbor. The result is even more straightforward here: Seeking FDA approval and performing clinical trials for FDA approval both fall squarely within the safe harbor's plain text.

This Court's decisions confirm the same. For example, in *Classen*, this Court held that the defendant's "clinical activities and FDA submissions" for a supplemental new drug application ("sNDA") to change the label (to address certain impacts) "are exempt from infringement under the safe harbor provision" as a matter of law. 786 F.3d at 897. So too here. Like in *Classen*, Avadel expects to file an sNDA to change the label (to add an IH indication) and may conduct additional clinical trials to support that application. Therefore, like in *Classen*, that conduct is "clearly … within the scope of the safe harbor" as a matter of law. *Id.*

This Court has likewise concluded that the safe harbor applies "regardless of the defendant's intent or purpose behind the otherwise infringing act," *Edwards*, 96 F.4th at 1356; *see Abtox, Inc. v. Exitron Corp.*, 122 F.3d 1019, 1030 (Fed. Cir. 1997), *as amended on reh'g*, 131 F.3d 1009 (Fed. Cir. 1997), and that the safe harbor "is

not restricted to pre-approval activities," *Momenta Pharms., Inc. v. Amphastar Pharms., Inc.*, 686 F.3d 1348, 1358-59 (Fed. Cir. 2012). And there are numerous other examples where this Court assessed the safe harbor's application as "an issue of law" where "the pertinent facts [we]re not in dispute." *Proveris Sci. Corp. v. Innovasystems, Inc.*, 536 F.3d 1256, 1260 (Fed. Cir. 2008); *see, e.g.*, *Amgen Inc. v. ITC*, 565 F.3d 846, 854 (Fed. Cir. 2009) (resolving "whether the safe harbor of § 271(e)(1) applies as a matter of law, and whether all of the [accused product] was entitled to the protection of the safe harbor"); *Abtox*, 122 F.3d at 1027-28 (deciding "legal question of whether section 271(e)(1) precludes infringement … [b]ecause this issue depends on statutory construction").

The answer is straightforward here. Following the district court's clarification, Appx38-44, the injunction's scope is not in dispute. And it is apparent as a matter of law that the enjoined activities come within the statutory safe harbor.

2. Jazz next argues that Avadel did not show that seeking FDA approval and performing clinical trials are "reasonably related" to the "development and submission of information" to FDA. Jazz Br. 44-50. But, again, the injunction on its face prohibits activities that are not just "reasonably related" to developing and submitting information to FDA; they *are* the development and submission of information to FDA and fall within the safe harbor as a matter of law. *Supra* at 3-5;

Avadel Br. 21-25, 28-29. At minimum, they are "reasonably related." *See id.*; *Edwards*, 96 F.4th at 1352-53; *Classen*, 786 F.3d at 897.

a. Jazz takes the remarkable position that the safe harbor is "silent on seeking FDA approval." Jazz Br. 54. That is plainly wrong. To obtain FDA approval for a new indication, as noted, Avadel will submit a supplemental new drug application. *See* 21 C.F.R. § 314.70(b) (describing "[c]hanges requiring supplement *submission* and approval prior to distribution" (emphasis added)); *id*. § 314.70(b)(2)(v) (requiring "supplement" for "labeling changes"); *id*. § 201.57(c)(2) (labeling must include "[i]ndications and usage").[1] That is unquestionably a "submission of information" to FDA—that is, expressly protected by the safe harbor. 35 U.S.C. § 271(e)(1). In *Classen*, for example, this Court held that such supplemental applications "seeking the FDA's approval to revise the label of their products" are "FDA submissions" that "clearly fall within the scope of the safe harbor." 786 F.3d at 897. Here, Avadel's anticipated submission of its supplemental application for an IH indication is just as clearly within the safe harbor. And Congress has decreed that "no injunctive or other relief" can prohibit it. 35 U.S.C. § 271(e)(3).

[1] *See also* FDA, *Guidance for Industry: Changes to an Approved NDA or ANDA* 24 (Apr. 2004), https://www.fda.gov/files/drugs/published/Changes-to-an-Approved-NDA-or-ANDA.pdf ("Changes based on postmarketing study results, including … labeling changes associated with new indications and usage" "must be submitted as a prior approval supplement.").

That is further confirmed by Section 271(e)(2), which states that it is an act of infringement "to submit" certain drug applications. This paragraph "define[s] a new (and somewhat artificial) act of infringement for a very limited and technical purpose that relates only to certain drug applications." *Eli Lilly*, 496 U.S. at 676. Absent Section 271(e)(2), such FDA submissions would be non-infringing under the Section 271(e)(1) safe harbor. *Id.* at 678. This underscores that FDA applications are, of course, "submission[s] of information" to FDA under Section 271(e)(1).

Jazz argues that there is "no reason" to conclude that "enjoining the FDA from approving an application under [Section] 271(e)(4)(A) for infringement under Section 271(e)(2) is permissible, but enjoining … asking the FDA for that very same approval is wrong." Jazz Br. 54. But Congress already addressed this: Submission of information to FDA, e.g., seeking FDA approval, is expressly within the safe harbor and *cannot be enjoined*. *See* 35 U.S.C. § 271(e)(3). Against that backdrop, Congress carved out (per Section 271(e)(2)) that submission of certain applications is nonetheless an "act of infringement," but the available remedies (per Section 271(e)(4)) include delaying "the effective date of any approval" until the patent expires—*not* enjoining the mere submission of the application.

Moreover, even apart from the safe harbor, the submission of an FDA application is not "mak[ing], us[ing], offer[ing] to sell, or sell[ing] any patented invention" under Section 271(a). *Id.* § 271(a); *see* Avadel Br. 24-25. That is clear

as a matter of plain meaning. And it is also the only reading that accords with the fundamental First Amendment right to petition administrative agencies like FDA. Avadel Br. 25. Jazz has no substantive response. Jazz apparently believes that submitting *information* to FDA *about* a patented invention is a "use" of that patented invention. It is not—any more than submitting briefing about the patented invention to this Court is a "use" of the patented invention. Jazz's strained statutory reading echoes its ill-fated attempt to contort the statutory Orange Book scheme, seeking to recast a patent for a database *storing information* about a drug into a "method of using" the drug. This Court rejected that effort, *see Jazz*, 60 F.4th at 1380-81, and should reject this one too. But even if submitting an FDA application were (counterintuitively) a "use" of the patented invention under Section 271(a), it falls within the safe harbor of Section 271(e)(1).

b. When it comes to clinical trials, Jazz contends that the safe harbor protects only activities that are *solely* related to the development and submission of information to FDA—and indeed are *required* for regulatory approval. Jazz Br. 44-48. According to Jazz, the statutory term "solely" means that activity performed for other "'purposes … would not be exempt.'" Jazz Br. 48 (quoting *Edwards*, 96 F.4th at 1358 (Lourie, J., dissenting)). This Court recently settled the issue in *Edwards* and rejected the same statutory interpretation that Jazz embraces: "It is *not* that the use must *only* be reasonably related to the development and submission of

information to the FDA." 96 F.4th at 1353 (first emphasis added). Rather, the safe harbor protects any "acts or uses that bear a reasonable relation to the development and submission of information to the FDA." *Id.* at 1353; *see id.* at 1350-51 (holding that activities for incentivizing doctors to participate in clinical studies—there, importing otherwise infringing products to a medical conference—are within the safe harbor). Jazz implicitly recognizes its argument is foreclosed, relying on the *Edwards* dissent and a cert petition seeking to overturn *Edwards*. Jazz Br. 48 & n.5.

But this case is far more straightforward than *Edwards*, and even under Jazz's improperly heightened standard, its argument still fails. As to future clinical trials, the injunction sweeps in *even* trials that could later be required for FDA approval. After Avadel completes the REVITALYZ trial and submits those results with its FDA application, FDA will decide "if more information is necessary," which might require Avadel to "submit new information."[2] Sometimes, "FDA requires additional studies" "before the drug can be approved for marketing."[3] Moreover, Avadel might well need to conduct additional trials even before submitting its application. But the

[2] FDA, *FDA's Drug Review Process: Continued* (Aug. 24, 2015), https://www.fda.gov/drugs/information-consumers-and-patients-drugs/fdas-drug-review-process-continued.

[3] FDA, *Step 4: FDA Drug Review* (Jan. 4, 2018), https://www.fda.gov/patients/drug-development-process/step-4-fda-drug-review.

injunction categorically precludes Avadel from pursuing any and all such trials necessary for approval.

As to the open-label safety extension ("OLE") portion of Avadel's currently ongoing REVITALYZ study, Jazz argues it was unnecessary. Jazz Br. 45-46. But the OLE is a critical component of the study both to incentivize participation and to generate important safety data—the REVITALYZ protocol calls for collecting data on all "safety endpoints," including adverse events, through this OLE period. *See* Avadel Br. 9-11, 17, 21-24.

Regardless, Jazz's argument misses the mark. Jazz recognizes that "the currently-ongoing [REVITALYZ] IH Trial" is "required to obtain approval for IH." Jazz Br. 46; *see id.* at 58 ("To request IH approval for Lumryz, Avadel must submit … information regarding the results of Avadel's IH Trial."). And, as Jazz does not contest, the OLE period is included in the protocol that *FDA approved* for the REVITALYZ trial. Avadel Br. 9-10. Therefore, OLE is at least reasonably related to the ongoing, required IH trial. In *Edwards*, this Court held that activities for incentivizing doctor participation in trials were sufficiently "reasonably related" to the FDA regulatory process to fall within the safe harbor. 96 F.4th at 1351. The inquiry did not (as Jazz would have it) turn on whether those incentivizing activities were independently "necessary" for FDA approval. *Contra* Jazz Br. 45-47. Here, the OLE is even more "reasonably related" because (unlike the *Edwards* activities)

the OLE is *in* the FDA-approved study protocol itself and provides not just important incentives but critical safety data.

As a fallback, Jazz argues that Avadel did not show that future clinical trials and the OLE portion of the currently-ongoing trial are "*not solely* related to commercial activity." Jazz Br. 48 (citing *Edwards*). That argument fails too. As discussed, future trials may be required by FDA, and the FDA-approved protocol for the ongoing REVITALYZ trial—which is "required to obtain approval for IH" (Jazz Br. 46)—includes an OLE portion. *Supra* at 12-13. Plus, the patients enrolled in the REVITALYZ trial "are not charged for the treatment they receive," including "in the open label extension portion" of the clinical trial. Appx7587 (Gudeman Decl. ¶ 2). Indeed, "study treatments at no cost to patients is customary in clinical trials and consistent with industry practices." Appx7587 (Gudeman Decl. ¶ 3).

At base, Jazz does not show that the enjoined activities are "wholly unrelated to any FDA submission." *Edwards*, 96 F.4th at 1355. Nor could it. As discussed, these activities are not only reasonably related to but *are* the development and submission of information for FDA under the safe harbor.

3. Next, Jazz asserts that the Lumryz dosage form does not meet the "safe harbor's 'patented invention' requirement, as opposed to being a research tool used in the FDA approval process." Jazz Br. 50-53. According to Jazz, the safe harbor cannot be invoked to "expand the use of an infringing product" that is already FDA-

approved and commercially marketed. *Id.* at 51. That argument is unfounded. Avadel Br. 30-31. Avadel's use of the Lumryz dosage to secure FDA approval for an IH indication *for use of the Lumryz dosage* plainly meets the safe harbor's "patented invention" requirement. *See id*.

This Court has rejected Jazz's categorical rule that an already approved product cannot be subject to the safe harbor, finding that "the plain language of the statute is not restricted to pre-approval activities" and holding that "post-approval studies" can fall within the safe harbor. *Momenta*, 686 F.3d at 1358-59. Here the safe harbor's application is even clearer, because the activities relate to seeking approval for a new indication for a previously approved drug.

Under Jazz's incorrect view of the statute, such activities would never be protected by the safe harbor, even where (as here) FDA approval is undisputedly required for an additional indication. That is not the law. Indeed, *Classen* rejects Jazz's argument. *Classen* found that "post-approval scientific studies and clinical trials to support 'supplemental' new drug applications, seeking the FDA's approval to revise the label of their products … serve similar purposes as pre-approval studies in ensuring the safety and efficacy of approved drugs." 786 F.3d at 897 (citing 21 C.F.R. § 314.70). Because such studies are "an integral part of the regulatory approval process," *Classen* held that they are "'reasonably related to the development and submission of information' under the FDCA, 35 U.S.C.

§ 271(e)(1), and are therefore exempt from infringement liability" as a matter of law. *Id.* The same is true here.

Jazz also wrongly asserts that there are "no regulatory barriers to market entry upon patent expiration." Jazz Br. 52-53 (quoting *Proveris*, 536 F.3d at 1265). To enter the IH market, Avadel must first seek FDA approval by submitting a supplemental new drug application—exactly what the injunction prevents until Jazz's patent expires. And it is no answer for Jazz to observe that Avadel can pursue FDA approval "upon patent expiration." Jazz Br. 53. Approval can take several months—so that is precisely the "improper patent term extension" that Congress enacted the safe harbor to eliminate. *Contra id*. As this Court has explained, "[b]y permitting the testing and regulatory approval process to begin *well before a controlling patent had run its course*, Congress must have intended to allow competitors to be in a position to market their products as soon as it was legally permissible." *Telectronics Pacing Sys., Inc. v. Ventritex, Inc.*, 982 F.2d 1520, 1525 (Fed. Cir. 1992) (emphasis added); *see also Classen Immunotherapies, Inc. v. Biogen IDEC*, 659 F.3d 1057, 1072 (Fed. Cir. 2011) ("facilitate market entry upon patent expiration").

Proveris is not to the contrary. There, this Court held that the safe harbor did not protect the marketing and sale of a device that was "used in the development of FDA regulatory submissions, but [wa]s not itself subject to the FDA premarket

approval process." 536 F.3d at 1265. The defendant was "not a party seeking FDA approval for a product in order to enter the market to compete with patentees." *Id*. But here, an IH indication for the Lumryz dosage (which Avadel stipulated infringes under the district court's claim construction) *is* subject to FDA premarket approval, and Avadel *is* seeking FDA approval for an IH indication to enter a market to compete with Jazz. The safe harbor applies.

4. Unable to circumvent the safe harbor, Jazz now insists that *even if* the activities fall within the safe harbor (and are thus non-infringing) the district court could enjoin them prophylactically to prevent other conduct that does infringe (i.e., the future, hypothetical marketing and sale of LUMRYZ for IH). Jazz Br. 57-60.

Jazz has not made this argument before. For good reason: the statute expressly forecloses it. Section 271(e)(3) provides that safe harbor conduct *cannot* be enjoined: "no injunctive or other relief may be granted which would prohibit the making, using, offering to sell, or selling within the United States or importing into the United States of a patented invention under [Section 271(e)(1)]." As this Court has held, "[c]onduct within the ambit of section 271(e)(1) … cannot be enjoined pursuant to section 271(e)(3)." *Eli Lilly & Co. v. Medtronic, Inc.*, 872 F.2d 402, 405 (Fed. Cir. 1989), *aff'd*, 496 U.S. 661 (1990). That is why "*no* injunction may issue until the § 271(e)(1) exception has been adjudicated and ruled out." *Eli Lilly & Co. v. Medtronic, Inc.*, 915 F.2d 670, 674 (Fed. Cir. 1990).

Even putting aside that glaring problem, Jazz is also wrong that "requesting FDA approval for IH would *unavoidably result* in marketing Lumryz for IH." Jazz Br. 57-58 (emphasis added). FDA has to exercise its scientific judgment and actually approve that use *before* Avadel can market Lumryz for IH. *Supra* at 11.[4] So the statutory scheme already rejects the notion that merely seeking and receiving FDA approval constitutes marketing. And precedent forecloses Jazz's argument that "[i]nclusion of a non-narcolepsy indication (*e.g.*, IH) on the Lumryz label constitutes marketing" per se. Jazz Br. 58. Again, *Classen*: "[P]lacing the *information* submitted to the FDA on the product label after sNDA approval generally cannot be an infringement. Information obtained from exempt activities does not cease to be exempt once the sNDA is approved. It is a requirement of law that a drug product contains the labeling approved by the FDA." 786 F.3d at 899. As *obtaining* FDA approval is not marketing, even less so is *seeking* FDA approval.

In short, the district court's injunction improperly enjoins conduct that falls within the statutory safe harbor, and nothing in Jazz's response shows otherwise.

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[4] Indeed, because Jazz's product, Xywav, has orphan drug exclusivity for IH until 2028, FDA must determine that Lumryz is clinically superior for treating IH before Avadel can market it. *See, e.g.*, 21 C.F.R. §§ 316.3(b), 316.20(a), 316.34; FDA, *Frequently Asked Questions (FAQ) About Designating an Orphan Product* FAQ #10 (May 11, 2023), https://www.fda.gov/industry/designating-orphan-product-drugs-and-biological-products/frequently-asked-questions-faq-about-designating-orphan-product.

B. The Question Whether The District Court's Injunction Exceeds Its Authority Is Properly Before This Court

Lacking any substantial arguments on the merits, Jazz leads with waiver. That is deeply ironic, as Jazz itself expressly, repeatedly disavowed attacking safe harbor activity. *See* Avadel Br. 27, 29.

1. Jazz, Not Avadel, Waived

In Jazz's operative complaint (its amended complaint filed June 9, 2023, after FDA's May 1, 2023 approval of Lumryz to treat narcolepsy), Jazz focused on Avadel's intent to "commercialize" Lumryz—including by, for instance, "import[ing] into the United States commercially manufactured batches" of Lumryz. Appx10001-10009 at Appx10006 (Compl. ¶¶ 27, 29). As a result, Jazz alleged that the "*commercial* manufacture, use, offer for sale, sale, and/or importation" of Lumryz constituted infringement. Appx10007 (Compl. ¶ 34) (emphasis added). But Jazz also specifically disclaimed infringement as to any "acts expressly exempted by 35 U.S.C. § 271(e)(1)." Appx10008 (Compl., Prayer for Relief ¶ D); *cf.* Appx10007 (Compl. ¶¶ 30-32) (alleging infringement under 35 U.S.C. § 271*(a)-(c)*). As Avadel explained to the district court, "Jazz has not contended that Avadel has engaged in any … activities [exempted by Section 271(e)(1)] or that they would form the basis of a damages claim." Appx7740-7744 at Appx7741 n.2. Jazz did not disagree. Nor did Jazz seek to further amend its complaint.

Moreover, at the injunction hearing, after Avadel explained why the safe harbor applies to seeking FDA approval and performing clinical trials (and the district court seemed to agree), Jazz offered no explanation to the contrary. Avadel Br. 13. Instead, Jazz expressly stated that "[w]e're not seeking to [e]njoin … clinical trials." Appx9101. Then, if there were any doubt, Jazz's post-hearing submission removes it: "Jazz *has never disputed* that Avadel could conduct those studies" for "idiopathic hypersomnia ('IH')." Appx7367 n.1 (emphasis added). Avadel pointed out this clear waiver in its opening brief, *see* Avadel Br. 29, and Jazz did not respond.

This illustrates why Jazz's claims of "extreme prejudice" ring hollow. Jazz Br. 33. Jazz cannot be prejudiced where it repeatedly admitted that it was not seeking to enjoin clinical trials—and where it could not have proceeded otherwise given the clear-cut safe harbor protection.

2. Avadel Raised The Safe-Harbor Exception In The Injunction Proceedings

Jazz argues Avadel waived its safe-harbor argument for three reasons. None has merit.

a. First, Jazz claims that the safe harbor provides an affirmative defense that Avadel failed to plead or prove. Jazz Br. 30-33. That misapprehends the issue. The question here is whether the district court exceeded its authority under Federal Rule of Civil Procedure 65 and 35 U.S.C. § 283 by enjoining activity that "clearly" falls under the statutory safe harbor. *See Classen*, 786 F.3d at 897; Avadel Br. 26-27.

This does not depend on resolution of any fact issue, and does not impact the jury's infringement verdict; rather, it goes to the unlawful scope of the injunction, which improperly sweeps in safe harbor conduct.

This Court has never held that the safe harbor must be raised as an affirmative defense. To the contrary, this Court has resolved it as a matter of law even in cases where no affirmative defense was pleaded. In *Classen*, for example, although the defendant did not raise an affirmative safe harbor defense, this Court held that the safe harbor applied to activities (indistinguishable from the ones here) for performing clinical studies and submitting an application to FDA. 786 F.3d at 897-98; *see generally* Elan Answer, *Classen Immunotherapies, Inc. v. King Pharms., Inc.*, 466 F. Supp. 2d. 621 (D. Md. 2006) (No. 04-cv-03521), Dkt. 20.

That makes sense. Unlike the patent infringement "defense[s]" enumerated in Section 282, the safe harbor of Section 271(e)(1) is an exception to infringement. Section 271(a) defines certain acts as infringement "*[e]xcept* as otherwise provided in this title," and Section 271(e)(1) provides that certain acts "shall not be" infringement in the safe harbor. 35 U.S.C. § 271(a), (e)(1) (emphasis added); *see Valeant Pharms. N. Am. LLC v. Mylan Pharms. Inc*., 978 F.3d 1374, 1381-82 (Fed. Cir. 2020) (safe harbor defines "acts[] which otherwise may have been infringing to be non-infringing"); 5 Donald S. Chisum, *Chisum on Patents* § 16.03[1] (2024, online) ("Congress added Section 271(e) to the Patent Act providing a special

statutory testing use exemption."). And the issue here is the unlawful scope of the injunction: The district court improperly enjoined safe harbor conduct that is non-infringing as a matter of law. *Supra* at 3-17; Avadel Br. 21-26.

To be sure, it might be appropriate to raise the safe harbor at the pleading stage or on summary judgment where (unlike here) the plaintiff pursues infringement of safe harbor conduct such as clinical trials. In *Merck*, for example, the complaint focused on alleged infringement through providing "financial and other support for … past and presently ongoing scientific research" and referred to "infringing scientific research." Compl. ¶ 9, *Integra LifeSciences I Ltd. v. Merck KGaA*, 1999 WL 398180 (S.D. Cal. 1999) (No. 96-CV-1307); *see also Classen*, 786 F.3d at 896 (plaintiff alleged defendant infringed "by conducting a clinical study on the bioavailability of Skelaxin and submitting the results to the FDA to revise the Skelaxin product label"); *Trutek Corp. v. Bluewillow Biologics, Inc.*, 2022 WL 20689596, at *1-2 (E.D. Mich. June 2, 2022).

But there was no need to do so based on Jazz's complaint here. Jazz alleged infringement based on Lumryz's commercial launch and expressly carved out safe harbor activities. *Supra* at 18-19. As discussed, Avadel raised the safe harbor issue in the injunction proceedings, and neither Jazz nor the district court suggested the issue was not properly presented. Instead, Jazz admitted that it was not seeking to enjoin clinical trials, and subsequently confirmed that it "*ha[d] never disputed* that

Avadel could conduct those [IH] studies." Appx7367 n.1 (emphasis added). Jazz cannot now insist that Avadel should have raised the issue sooner.

b. Second, Jazz argues that Avadel waived any safe harbor protection by "stipulating to infringement without including an exemption for any alleged safe harbor activities that it planned." Jazz Br. 33. But, again, Jazz itself exempted from the scope of its infringement claim any "acts expressly exempted by" the statutory safe harbor. Appx10008; Avadel Br. 28 n.8. Moreover, the stipulation acknowledges infringement "pursuant to 35 U.S.C. § 271(a)," Appx4312, and Section 271(a) itself exempts the safe harbor activities of Section 271(e)(1) as non-infringing as a matter of law. The stipulation nowhere suggests that Avadel meant to silently agree to transform those statutorily non-infringing activities into infringing ones. When Avadel entered into this stipulation in February 2024, Appx4311-4313, Lumryz had already launched commercially in June 2023. Appx9257 (495:10-12). So Avadel was engaged in commercial sales at that point, which is activity that does not fall within the safe harbor. The stipulation covers such activities, not exempt safe harbor activities.

c. Third, Jazz argues that Avadel waived because it did not reference the safe harbor in its injunction briefing. Jazz Br. 37-39. However, although Jazz's proposed injunction includes language prohibiting seeking FDA approval or performing future clinical trials, Jazz's injunction briefing offers little meaningful argument for why

enjoining those activities would be lawful. *See* Appx4578 (referencing this request only in passing); *cf. Medtronic, Inc. v. Teleflex Life Scis. Ltd.*, 86 F.4th 902 907 (Fed. Cir. 2023) (requiring arguments to be "adequately developed" in briefing (citation omitted)). Avadel opposed the injunction in full, Appx5652-5678, and repeatedly raised the safe harbor at the hearing. Avadel Br. 13, 28-29; *see* Appx9064-9066, Appx9077, Appx9079-9080, Appx9087, Appx9105.

Neither the district court nor Jazz suggested that the issue was not properly presented. To the contrary, the district court seemed to accept that Avadel's clinical studies and regulatory submissions are protected. Appx9066 (66:24-25). Jazz likewise provided no reasons why they would fall outside the safe harbor, and admitted it was not seeking to enjoin clinical trials. Appx9100-9101. And, as discussed, Jazz thereafter confirmed that it "never disputed" that Avadel could conduct studies for IH. Appx7367 n.1. Jazz waived, not Avadel. *Supra* at 18-19.

d. Jazz also argues that this Court considering the proper interpretation of the safe harbor would "unduly prejudice Jazz." Jazz Br. 39-42. But that argument presumes the issue requires factual development. It does not; in this case, the issue is statutory interpretation, which this Court can decide as a matter of law. S*upra* at 7-17. And as discussed, Jazz itself exempted safe harbor conduct. *Supra* at 18-19. So Jazz's representations (at 40-41) that it would have pursued a different (unspecified) strategy are unavailing. No amount of discovery or attorney argument

could show that Avadel's actions in seeking FDA approval and performing clinical trials for it are outside the safe harbor and fair game for an injunction.

e. Notably, Jazz raised this same waiver argument in opposing a stay pending appeal in the district court. But the court did not find waiver, even as it clarified the injunction's scope and rejected some of Jazz's attempted expansion. *See* Appx7542-7545; Appx40. Jazz raised the waiver argument again in opposing a stay in this Court, ECF No. 19 at 7-10, but this Court likewise identified no such concerns, even as it granted a partial stay, ECF No. 30 at 3. Jazz leads with waiver once more because its merits arguments are profoundly weak and contrary to governing law.

3. This Court Can, And Should, Address This Straightforward Legal Issue In Any Event

Even if there were waiver, this Court should exercise its discretion to interpret the safe-harbor provision. *See Interactive Gift Express, Inc. v. Compuserve Inc.*, 256 F.3d 1323, 1344-45 (Fed. Cir. 2001) (collecting cases). This Court has discretion to consider an issue of "statutory interpretation, a purely legal issue," even if it were "not … raised below or in an appellant's opening brief." *Bozeman Fin. LLC v. Fed. Rsrv. Bank of Atl.*, 955 F.3d 971, 974-75 (Fed. Cir. 2020); *see also, e.g.*, *Cemex, S.A. v. United States*, 133 F.3d 897, 902 (Fed. Cir. 1998). Here, the case turns on a straightforward legal issue—interpretation of the safe-harbor provision, which the district court had the opportunity to address but declined. *Compare* Appx9064-

9066, Appx9077, Appx9079-9080, Appx9087, *and* Appx9105 (raising the safe harbor), *with* Appx1-44 (no mention of safe harbor). It is ripe for resolution.

That is especially appropriate here because "the proper resolution is beyond any doubt," *Singleton v. Wulff*, 428 U.S. 106, 121 (1976), and "injustice [would] otherwise result," *Hormel v. Helvering*, 312 U.S. 552, 557 (1941). The injunction is unprecedented: Jazz has cited no case—and Avadel found none—where a district court so clearly contravened the plain text of the safe harbor. *Cf. Classen*, 786 F.3d at 897-98 (holding district court properly held that the same type of activities were non-infringing as a matter of law under the safe harbor). And given the clarity of Congress' command in Section 271(e), the Court should correct that error here.

II. THE DISTRICT COURT'S LEGALLY FLAWED ANALYSIS OF THE *EBAY* FACTORS WAS AN ABUSE OF DISCRETION

The district court's injunction also suffers from a series of errors in its analysis of the *eBay* factors, and should be reversed for that reason too. Avadel Br. 32-39.

1. *Irreparable harm and lack of adequate remedy.* Jazz cannot establish these factors for two reasons: (i) the district court enjoined conduct that is non-infringing as a matter of law and (ii) any harm to Jazz from marketing Lumryz to IH patients is entirely hypothetical and speculative at this point. *Id.* at 33-35.

First, Jazz has to show that "it is irreparably harmed *by the infringement*," which requires a "'causal nexus'" establishing that "the *infringement* causes the harm." *Apple Inc. v. Samsung Elecs. Co.*, 809 F.3d 633, 639 (Fed. Cir. 2015)

(emphases added). Because the safe harbor renders seeking FDA approval and clinical trials for an IH indication non-infringing as a matter of law, *supra* at 7-17, Jazz cannot demonstrate irreparable harm from these activities. Tellingly, Jazz's only response is that Avadel waived its safe harbor argument. Jazz Br. 63-64. But that is wrong. *See supra* at 18-24; *see also* Appx5668-5669 (citing *Apple*).

Second, Jazz is wrong that "seeking FDA approval would necessarily result in marketing Lumryz for IH." Jazz Br. 64. Indeed, Jazz admitted that "[w]e don't even know if [Lumryz is] going to get approval" for IH. Appx9101. So the "harm … of being forced to compete" in the IH market remains hypothetical—even on Jazz's terms, it is not seeking FDA approval but receiving it that leads to competition in the IH market. Jazz Br. 62-63. More fundamentally, the regulatory scheme distinguishes between seeking FDA approval for a product and marketing it. *Supra* at 11, 17. Seeking and receiving FDA approval are *prerequisites* to marketing (and commercialization more generally), not a *form of* marketing.

2. *Balance of the equities.* The district court also incorrectly analyzed the balance of the equities. Avadel Br. 36-37. If the district court were right that Avadel cannot show injury with respect to the IH market because it lacks FDA approval for this indication, Appx27, it follows that Jazz could not show injury with respect to the IH market either. Again, as Jazz admitted, "[w]e don't even know if [Lumryz is] going to get approval" for IH yet. Appx9101. So the district court's finding that

Jazz faced a substantial hardship in "compet[ing] against its own patented invention" does not hold up. Appx27 (citation omitted).

Because of the way that FDA approval works, the district court also conferred an indirect extension of Jazz's patent term while failing to consider this problem. Avadel Br. 36; *supra* at 15. As the injunction prohibits submitting a supplemental application to FDA, it necessarily extends Jazz's status as the only approved IH treatment beyond the life of Jazz's patent. As the Supreme Court has recognized, there is an "often substantial period until regulatory approval [i]s obtained" after an application is submitted. *Eli Lilly*, 496 U.S. at 670. So it is unclear what distinction Jazz is trying to draw between "'lin[ing] up'" approval and "asking for FDA approval." Jazz. Br. 68-69. In the real world, that distinction makes no sense: To get approval for an IH indication, Avadel has to submit a supplemental NDA to FDA with clinical study data—which the injunction prohibits. *See supra* at 6, 8.

Plus, in this case, Avadel's approval for narcolepsy—and, consequently, its clinical work for IH—was already delayed due to Jazz's improper listing of a computer-systems patent in FDA's Orange Book. Appx5977 (Divis Decl. ¶ 13); Appx9076 (76:11-19); *see Jazz*, 60 F.4th 1373. That impropriety ought to influence the equities, but the district court did not consider it. Appx27.

3. *Public interest.* Finally, the district court erred in assessing the public interest. Avadel Br. 37-39. To start, the district court *did* place the burden on Avadel

when it came to the public interest. *Contra* Jazz Br. 70-71; *see* Appx30 ("Avadel has not shown …."), Appx31 ("Avadel had the burden … [and] Avadel failed to show …."). That was error. Avadel Br. 37-38. And shunting that burden onto Avadel was especially misplaced because the district court ruled less than a month after Avadel had started its REVITALYZ trial for IH—which means that Avadel had not yet been able to show all of the "distinct benefits" that Lumryz offers to patients with IH. Appx30; *cf.* Jazz Br. 71. But the injunction cuts off Avadel from conducting any further studies, which may become necessary for FDA approval.

Moreover, the district court itself found that the public interest weighed heavily in Avadel's favor when it came to Lumryz's treatment of narcolepsy, relying on FDA's conclusion that Lumryz is clinically superior to Jazz's products because its once-nightly dosing makes a major contribution to patient care. Appx17-23. By the same logic, it is impossible for the district court to accurately assess the public interest when it short-circuits FDA's assessment of using Lumryz to treat IH. Of course, after FDA weighs in, the district court could assess the facts at that time. *See* Appx9077-9078. But Jazz insists FDA should not have that chance.

This is consistent with Jazz's approach throughout this litigation in seeking to block FDA's consideration and approval of clinically superior treatments that can have life-changing benefits for patients. This Court already rejected Jazz's attempt to improperly list a patent in FDA's Orange Book, clearing the way for FDA to

approve Avadel's once-nightly treatment for narcolepsy (the only one FDA has approved). *See Jazz*, 60 F.4th at 1380-81. Recently a court rejected Jazz's attempt to undo that FDA approval, explaining that Jazz improperly challenged "an 'area of special expertise' of the FDA" and that "it is not for the judicial branch to undertake comparative evaluations of conflicting scientific evidence." *Jazz Pharms., Inc. v. Becerra*, 2024 WL 4625731, at *10, *25, *27 (D.D.C. Oct. 30, 2024). But here, Jazz succeeded in preempting FDA's expert evaluation, persuading the district court to determine the public interest prematurely.

Finally, Jazz asserts that there is no "manifest public interest in the clinical investigation and expert administrative review that goes into the FDA approval process" and that Avadel "seeks to elevate the rights of an infringer over the rights of an innovator, whom the law seeks to protect." Jazz Br. 72 (citation omitted). But that overlooks Congress's judgment: certain activities are non-infringing *per se* under the safe harbor and cannot be enjoined. That is what the law protects, but what the district court's injunction improperly prohibits.

CONCLUSION

The district court's orders enjoining Avadel should be reversed.

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Respectfully submitted,

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CERTIFICATE OF COMPLIANCE

Pursuant to Federal Rule of Appellate Procedure 32(g)(1) and Federal Circuit Rule 32(b)(3), I hereby certify that the foregoing document complies with the type-volume limitation in Federal Circuit Rule 32(b)(1) because it contains 6,990 words, excluding the exempted parts under Federal Rule of Appellate Procedure 32(f) and Federal Circuit Rule 32(b)(2).

I further certify that the foregoing document complies with the typeface requirements of Federal Rule of Appellate Procedure 32(a)(5)-(6) because this response was prepared using Microsoft Word 365 in 14-point Times New Roman font.

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